University of Virginia
HEALTH
SYSTEM

M.D./Ph.D. Program Newsletter

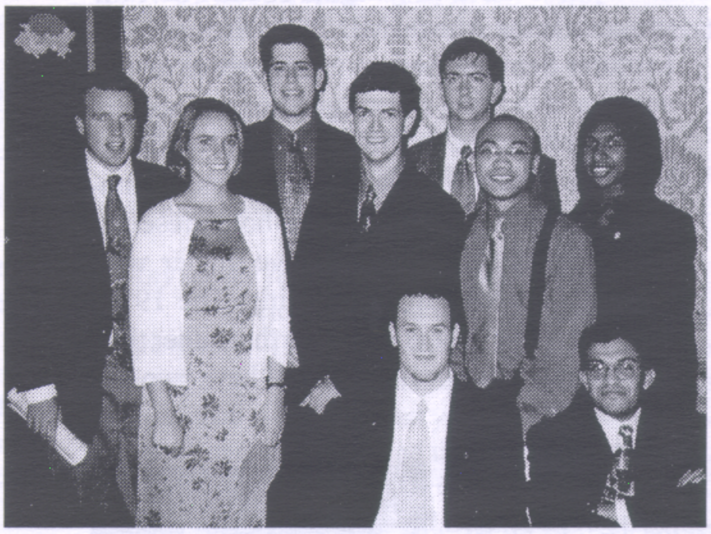
Volume 2, No. 1 Winter 2000

Words from Our Director

I want to take this opportunity to formally thank each of you for the superb efforts that you made in revitalizing our M.D./Ph.D. Program, and to congratulate you for the re-acquisition of the NIH Medical Scientist Training (MST) Program grant. The NIH site visitors were extremely impressed with you, and the improvements in our Program. Indeed, the grant review described the transformation of the Program as being "truly remarkable". Our success has clearly been the result of the efforts of many individuals. I am proud of our program, and its students. Whereas we have reason to celebrate, we do not want to rest on our laurels and need to continue to strive to improve the overall quality of our program. To begin this process, I would like to briefly review some of the things that we have done, and to outline my vision for the future of the Program.

Our new MST Program integrated curriculum is now in its second year and is working well. The changes in the curriculum were viewed very positively by the site visitors. First year students now take Grad Cell and Grad Biochemistry in place of the Medical School equivalents. We have also made some changes to the Doctor/Patient Illness (DPI) Course, and Gross Anatomy to better promote training of physician-scientists. For example, the Doctor/Patient Illness (DPI) Clinical Sessions include rounding with physician-scientists in the UVA Health System rather than with generalist preceptors in the community. DPI student groups include multiple MST Program students, and preceptors are selected who will embrace and support the goals of our Program. The Gross Anatomy Course has been modified by grouping MST Program students for dissections, and by inclusion of a special weekly review session that includes presentations by the MST Program students of research publications dealing with gross anatomy or modern biomedical imaging techniques/modalities. In addition to promoting development of MST Program students as physician-scientists, the integrated curriculum has also resulted in students acquiring 35 of the 56 topical GSAS credits needed for a Ph.D. prior to their entering graduate school. There is also much greater flexibility in selecting courses

(Continued on page 4)



The entering M.D./Ph.D. class was welcomed at the Dean's Reception held at Alumni Hall on Thursday, August 19, 1999. (L to R: front Tim Ciesielski, Rooshin Dalal, middle Stacey Sheasley, Brandon Kremer, Shawn Carbonell, Tresa Thompkins, back T.J. O'Neill, Mark Hoofnagle, Paul Sykes.) Not pictured: Shaharyar Khan

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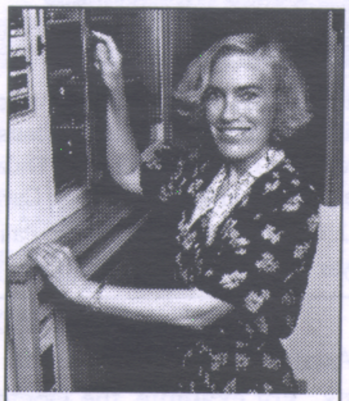
1999-2000 Distinguished Lecturers - Jonathan Stamler, M.D. Elaine Fuchs, Ph.D.

- MSK & RCI

One of the highlights of the MD/PhD program is the Annual MD/PhD Distinguished Lecturer Seminar Series. The purpose of this seminar is to bring a distinguished and accomplished physician/scientist to the University of Virginia to meet with faculty members and students during the day, give a one-hour presentation on their research, and have dinner with MD/PhD students in the evening. The 1999-2000 academic year is special in that rather than having only one speaker we will have two exceptional scientists present to us.



Dr. Elaine Fuchs
Howard Hughes Medical Institute
University of Chicago

On October 12th, 1999, we were fortunate to have Dr. Jonathan Stamler from the Howard Hughes Medical Institute at Duke University Medical Center come and speak to us not only about his revolutionary research on hemoglobin and nitric oxide (NO), but also on his views about being a physician-scientist. Stamler told us that although gas exchange occurs in the capillaries, most of the oxygen is released by hemoglobin before it reaches these microvessels. This deoxygenation causes an allosteric transition in S-nitrosohemoglobin, causing it to release the NO group. NO then mediates vessel relaxation and increases blood flow. Thus, he proposed that hemoglobin can sense the physiological oxygen gradient in tissues and use conformation associated changes to make local blood flow match tissue oxygen requirements. When asked about his secret for success, he said he does not think about it. He just does what he loves and tries to get through the day!

Get ready for April 11th, 2000, when we will be visited by Dr. Elaine Fuchs from the University of Chicago. Like Dr. Stamler, Dr. Fuchs is an investigator for the Howard Hughes Medical Institute. Among her many numerous awards and recognitions, she is a member of both the American Academy of Arts and Sciences and the National Academy of Sciences. In addition, Dr. Fuchs has recently been elected as President for the American Society of Cell Biology for 2000. Using human cell cultures and gene knockout technology, she focuses on the process of cell growth and differentiation of mammalian ectoderm into either epithelial skin cells or neurons. She also studies formation of the cytoskeleton in these cells. Dr. Fuchs' research not only focuses at the level of molecular, cellular, and developmental biology, but also relates to clinical medicine by her ability to define genes that are mutated in degenerative diseases that can occur in humans. We are very excited to hear her lecture titled, "Beauty is skin deep: Mechanisms of growth and differentiation in the skin."

Calendar of Events

March 21 - Research In Progress Dinner, Jordan 2a,b,c
April 11 - Distinguished Lecture Dr. Elaine Fuchs
April 18 - Research in Progress Dinner
May 13 - MSTP Graduation Party
June - MSTP Retreat

Alumni Focus - Dr. Alissa Weaver

Alissa Weaver, M.D., Ph.D., who graduated with UVA class of 1998 is currently a resident at Washington University. She has kindly shared with us her perspective on what life is like during residency.

Can you tell us where you are in your training and give us a description of your program?

I am a second year Laboratory Medicine Resident at Washington University (St. Louis) School of Medicine/Barnes-Jewish Hospital. This is the same as "Clinical Pathology," which does not include any Anatomic or Surgical Pathology, i.e. no autopsies or surgical specimens. I am being trained to be a director of a clinical laboratory and to be a research scientist. The clinical areas in which I receive training include Blood Banking, Hemostasis/Coagulation, Clinical Chemistry, Microbiology, Immunology, Molecular Diagnostics — basically anything that is assessed in a clinical laboratory. The time split for the residency is as follows: the first year is clinical, in which one rotates through the various clinical specialties, takes beeper calls, and gives clinical conferences. Then a variable amount of time is spent doing a postdoctoral fellowship in any of the research labs at Washington University. The hospital/department funds up to 2 years of this, after which time one has to obtain external support. The final year is clinical and spent on an "area of interest."

How did you chose this residency program and is it what you expected?

It is exactly what I expected. I chose this residency because I am interested in spending the majority of my time as a medical researcher. This residency is unique in enabling me to specifically train as a researcher, while also receiving clinical specialization and becoming licensed as a physician.

What do you like most about where you are now?

Washington University is a fabulous place to do research. Also, I really like my new lab — both the PI and the other members of the laboratory. I am currently doing a postdoctoral fellowship in John Cooper's laboratory, studying the mechanisms of dynamic rearrangements of the actin cytoskeleton during cellular migration.

Do you find that your current research relates in any way to your graduate work here at UVA?

Only in a general sense. My final and most successful graduate project was demonstrating that lipoprotein receptor-related protein (LRP) was involved in regulating cellular migration. My current research also focuses on molecular mechanisms involved in cellular migration.

Where do you see yourself in ten years?

Hopefully as a faculty member at a good university near the ocean.

What do you miss about UVA?

The Blue Ridge Mountains. A smaller, less chaotic hospital.

Any advice for current MD/PhD students here?

Decide what you want and go after it aggressively. Think realistically about how you are going to receive the training you need to compete in science — decide what your "split" between research and clinical is and think about whether it's tenable (50:50, 70:30, 100:0). We need more M.D. perspectives out there — M.D. scientists are a dwindling breed — so I hope people will continue to choose science. It's a wonderful field but competitive, so plan your attack ahead of time.

Recent Publications:

Weaver, A.M., Husaini, I.M., Mazar, A., Henkin, J., and S.L. Gonias, "Embryonic fibroblasts that are genetically deficinient in low density lopoprotein receptor-related protein demonstrate increased activiy of the urokinase receptor system and accelerated migration on vitronectin." *J. Biol. Chem. 272:14372-14379*, 1997.

Weaver, A.M., Lysiak, J.J., and S.L. Gonias, "LDL receptor family-dependent and independent pathways for the internalization and digestion of lipoprotein lipase-associated β-VLDL by rat vascular smooth muscle cells." *J. Lipid Research.* 38:1841-1850, 1997. (cover article).

Harthun, N.L., **Weaver, A.M.**, Brinckerhoff, L.M., Deacon, D.H., Gonias, S.L., and C.L. Slingluff, "Activated α2-macroglobulin reverses the immunosuppressive activity in human breast cancer cell-conditioned medium by selectively neutralizing transforming growth factor-β in the presence of interleuking-2." *J. Immunotherapy*. 21:85-94, 1998.

Hussaini, I.M., Brown, M.D., **Weaver, A.M.**, Carpenter, J, Karns, L.R., Vandenberg, S.R., and S.L. Gonias, "Stable antisense RNA expression neutralizes the activity of low-density lipoprotein receptor-related protein and promotes urokinase accumulation in the medium of an astrocytic tumor cells line," *Antisense and Nuceic Acid Drug Development*, 9:183-190, 1999.

From Our Director (cont. from pg. 1)

that are taken during the first year. For example, four of our first year students, have elected to take a Neuroscience selected topics research course (NESC 707) that parallels the Medical Neuroscience Course in place of the second semester of the Molecular Basis of Human Disease.

One of the most striking changes in the program is our recruiting and admissions process. We now have an early recruiting/admissions process that begins as soon as applications are received in August. Interviews begin in mid-October and offers to our top candidates are extended within one to two weeks. Most of you have participated in this process and have been a major part of its success. A special thanks to Shawn Carbonnel who has played a leadership role in heading up many of our recruiting efforts, and in fine tuning our admissions/recruiting policies and practices. There is nothing that is more valuable in trying to recruit students than for them to see how excited you are about our program. In brief, our new recruiting/admissions process involves an initial review by Dr. Brautigan, and myself plus one additional member of the Admissions Committee. Students are invited for a two day visit with the program paying all local expenses plus a $300 travel allowance. Students are interviewed by multiple faculty members, including many prospective mentors selected based on the student's interests, essays, etc. Faculty are asked to complete formal evaluations on each candidate and these are submitted to Dr. Owens and Brautigan. These are reviewed, and if there is an obvious consensus an offer is made. If there are questions regarding whether an offer should be made, additional consultations and discussions are done as appropriate to make a decision. Our philosophy is to extend an offer to any outstanding individual that we consider appropriate for our program. Unlike previously, we extend more offers than we have positions assuming that our yield rate will not be 100%. Thus far this year we have extended eleven offers. Based on my conversations with candidates over the last several weeks, I am confident that we will have another outstanding first year class join us this year.

One of the most satisfying aspects of my first 1 ½ years as Director has been to watch the evolution of camaraderie among MST Program students. As you well know, combined degree programs are extremely rigorous and it is extremely important that you identify a peer group for mutual support and interaction. Many of you will remember our very first research-in-progress session in May of 1998 where I was dismayed to find that many MST Program students did not know students that entered during a different year. This is in striking contrast to our program today as evidenced during the site visit when reviewers asked one of the two middle students groups to explain the research project of the individual sitting on their left. Students performed so well, that after going through half the group, the reviewers decided to go on to the next question.

An additional noteworthy change is that we have tried to get each student to carefully think about the integration of their research project, and their clinical interests as early as possible in the training period. This begins with the very first phone call that I make to potential recruits, and continues throughout the program. Indeed, one of the major goals of the clinical sessions in the DPI Course, and the selection of clinical faculty representatives on your MST Program individual student Advisory Committee is to insure that you gain clinical experience in perceived areas of interest very early in your training period and prior to selection of a Ph.D. mentor. The goal is to insure integration of thesis projects with clinical interests and your long-term career goals. We have also improved processes to help you in your selection of clinical clerkships upon return to medical school. As you know, timing of clerkships is critical since you are required to submit applications for residency programs in August of the year preceding your graduation. As such, you must complete clerkships in areas of perceived clinical interest before that time.

Although I am very pleased with the progress that we have made, we need to continue to improve

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Ideas and comments are welcome.

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M.D./Ph.D. Program Summer Retreat
Smith Mountain Lake, Virginia
June 25-26, 1999

the overall quality of our program. I see three major challenges. First, the Medical School is in the process of major reform of the medical curriculum. It is extremely important that the MST Program play a major role in this process to ensure that changes will further enhance training of physician-scientists. To do this, I have met on several occasions with Dr. Don Innes the Associate Dean for the Medical Curriculum and chair of the Medical Curriculum Committee. I have written several proposals that will be incorporated into the overall plan, and have had Dr. Petri appointed to represent the MST Program on Dr. Innes' committee. Although nothing is yet final, a positive aspect of the proposed curricular changes is that they will provide greater flexibility to all medical students to take elective courses during the first two years. An additional positive change is that many of the first and second year courses will incorporate new material that covers selected topics in biomedical research similar to what is done in our Molecular Basis of Human Disease Course. The idea is to promote appreciation of the biomedical research process and how it contributes to advances in medicine among all medical students.

A second major challenge will be to continue to expand the pool of applicants for our MST Program. Although our current pool includes many outstanding students, it needs to be further expanded. Our plans are to expand efforts to advertise our program to undergraduates, and premed advisors. Establishing referral networks with pre-medical advisors and former undergraduate research mentors is one of the most effective means of increasing our applicant pool. As such, I would strongly urge you to take a few minutes to contact these individuals, and tell them about our outstanding MST Program.

Finally, a major challenge will be to continue to look for ways to improve the overall efficiency of both MST Program and graduate training in general. I have recently prepared a Strategic Plan for Graduate Education within the School of Medicine that incorporates a variety of innovative ideas to improve the efficiency of graduate training. For example, one component involves setting up formal in depth technical courses/workshops, and/or better utilizing existing outside courses and workshops to assist students in mastering key technologies (e.g. protein purification, production of recombinant proteins, sub-cloning, expression array analyses, embryonic stem cell work, gene knockouts, etc.). The idea is to reduce excess loss of time working out a technique that may be routine in other labs. Additional revisions that are likely to be made are to enhance and expand training of students with regard to intellectual property rights and translational research. In addition, we hope to initiate new courses and training efforts with our Health Evaluation Sciences Department to better familiarize you, and our other graduate students with clinical research.

Gary Owens, Director

In summary, I think we have an absolutely fantastic M.D./Ph.D. Program that is among the best in the country. Moreover, there is good reason to believe that we will continue to get better. The school is in the midst of continued expansion of its biomedical research enterprise with construction of a new MR5 Research Building, plans for still another research building, and renovations of major new laboratory space. Major new hires have been made in clinical departments to enhance the number of clinician investigators, and an exciting new plan "The Clinical Investigator Advancement Program" has been implemented to better insure the success of our Clinician Investigators. This plan will undoubtedly improve the overall culture and climate for the success of physician-scientists at this institution, and in doing so will create new opportunities and resources for physician-scientist trainees. I want to end by saying that serving as your director has been one of the most enjoyable, and rewarding things that I have done in my entire professional career. Your intelligence, commitment, and enthusiasm are absolutely invigorating.

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